

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT (PCT Article 36 and Rule 70)

Applicant's or agent's file reference WO/171	<b>FOR FURTHER ACTION</b>		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP2004/001021	International filing date (day/month/year) 04.02.2004		Priority date (day/month/year) 06.02.2003
International Patent Classification (IPC) or both national classification and IPC C07C63/04, C07C65/32, C07C59/205, C07C311/29, C07C311/02; C07D207/32, C07D295/12, C07D209/42			
Applicant DOMPE S.P.A. et al.			

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 6 sheets.</p>	
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I    <input checked="" type="checkbox"/> Basis of the opinion</li> <li>II   <input type="checkbox"/> Priority</li> <li>III   <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV   <input type="checkbox"/> Lack of unity of invention</li> <li>V   <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI   <input type="checkbox"/> Certain documents cited</li> <li>VII   <input type="checkbox"/> Certain defects in the international application</li> <li>VIII   <input type="checkbox"/> Certain observations on the international application</li> </ul>	

Date of submission of the demand  01.09.2004	Date of completion of this report  25.05.2005
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  Menegaki, F Telephone No. +49 89 2399-8277



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP2004/001021

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-36 as originally filed

**Claims, Numbers**

1-15 filed with telefax on 16.03.2005.

**Drawings, Sheets**

1-4 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

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5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).  
*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

**6. Additional observations, if necessary:**

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

## 1. Statement

<b>Novelty (N)</b>	Yes: Claims	1-15
	No: Claims	
<b>Inventive step (IS)</b>	Yes: Claims	7,10
	No: Claims	1-6, 8, 9, 11-15
<b>Industrial applicability (IA)</b>	Yes: Claims	1-15
	No: Claims	

## 2. Citations and explanations

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP2004/001021

Documents (D1) WO 01/58852; (D2) WO 02/068377 differ from the present compounds due to the propionyl group compared with present acetic group;

(D3) Journal of Med. Chemistry, vol.24, 1981, p.998-1000, in particular specific compounds in Table 1 therein, differs from present Claim 7 due to the position of the benzoyl substituent.

In view of the specified definition of the diseases that can be treated using medicaments prepared with the present compounds as the active ingredient, novelty can be acknowledged over documents.

(D4) FR-A-1574570, in particular Examples II/V as well as Claims 2-17, 20, dealing with antiinflammatory agents;

(D5) Journal of Med. Chemistry vol.25, no.4, 1982, p.446-451, col.2, in particular antiinflammatory compound indomethacin therein. Both these prior art documents disclose similar antiinflammatory properties.

Therefore, the requirements of Art.33(2) PCT appear to be fulfilled for all Claims 1-15.

The problem underlying the invention is considered to be the provision of the novel 2-aryl acetic acid derivatives of formulas (I) according to Claim 1, which show IL-8 specific inhibiting activity without COX-inhibition. Documents (D1)/(D2) show structurally similar compounds having the same pharmacological profile and differing due to the additional CH<sub>3</sub>-group of the propionyl moiety, as well as the present group "Hy" in 2-position, which was not preferably or specifically disclosed in (D1)(D2).

Doc.(D1)/(D2) are not considered to be relevant prior art.

The Applicant has also clarified that the present pharmacological properties are different from the inflammatory activity disclosed in (D3) to (D5), which are no longer considered to be relevant prior art.

Nevertheless, for the acknowledgement of an inventive step per se on the basis of the claimed activity tested per se on p.16 of the description, the scope of the compounds of claimed formula (I) in Claims 1-6 appears to be very broad, as encompassing a huge number of 2-(2-Hy substituted aryl)-acetic acid derivatives, bearing

- (i) a further substituent group "R", which is not the same in m- and p-position of Ar=phenyl or 3- and 4-position when Ar=bicyclic, and/or
- (ii) different combinations of "R' ", depending on the definition of "Y".

The Applicant has prepared and tested only the compounds of Claims 7 and 10, and has supplied further test results with his letter of 16/03/2005 supporting the activity of certain specific examples.

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In view of the fact that minor structural differences such as the present acetyl or 2-Hy group can be essential for the claimed IL-8 inhibiting activity, the scope of the claimed substituent definitions in Claims other than 7 and 10 is considered to be too broad and speculative, appearing to go far beyond the possibilities explored by the Applicant. Therefore, the requirements of Art.33(3) PCT appear to be fulfilled for Claims 7, 10 but not for Claims 1-6, 8, 9 and dependent claims thereof 11-15.